

PATENT COOPERATION TREATY

PCT

REC'D 23 OCT 2001

EPO

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference X-12968		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/20824	International filing date (day/month/year) 14/09/2000	Priority date (day/month/year) 29/09/1999	
International Patent Classification (IPC) or national classification and IPC C07D409/14			
Applicant ELI LILLY AND COMPANY et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 03/04/2001	Date of completion of this report 06.07.2001
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Papathoma, S Telephone No. +49 89 2399 7536 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20824

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*)

Description, pages:

1-103 as originally filed

Claims, No.:

1-20 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

International application No. PCT/US00/20824

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/20824

No: Claims

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/20824

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

For the assessment of the present claims 12-14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: PATENT ABSTRACTS OF JAPAN vol. 018, no. 046 (C-1157), 25 January 1994 (1994-01-25) & JP 05 271220 A (AJINOMOTO CO INC), 19 October 1993 (1993-10-19)
- D2: WO 99 05140 A (MIKKELSEN IVAN ;LUNDBECK & CO AS H (DK); MOLTZEN EJNER KNUD (DK);) 4 February 1999 (1999-02-04)
- D3: EP-A-0 812 826 (LILLY CO ELI) 17 December 1997 (1997-12-17)

The application refers to piperidine derivatives of the formula I suitable for inhibiting the reuptake of serotonin and antagonizing the serotonin receptor.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/20824

1) Article 33(2) PCT

Although the prior art documents refer to similar compounds, the ones of the application were not disclosed in any of them. Therefore the compounds of the application, their pharmaceutical compositions, their uses and the methods of treatment comprising their administration are novel according to the Article 33(2) PCT.

2) Article 33(3) PCT

From the prior art documents D1 is considered to be the closest prior art, since its compounds, and particularly, the compounds 5, 22, 31, 32, 36, 37, 38, 39, 43, and 44, are the structurally closest more related compounds to the ones of the application and moreover they show antiserotonic activity.

However by the compounds of the application the R⁴ substituent can be an aryl, cycloalkyl etc. group, while the ones of D1 have in the corresponding position a CN group as substituent.

The CN-substitution of the compounds of D1 can not be considered to make obvious a substitution by a cyclic moiety (aryl etc.), as proposed in the application.

Therefore the compounds of the application, their pharmaceutical compositions, their uses and the methods of treatment comprising their administration are considered to be inventive according to the Article 33(3) PCT.

Re Item VI

Certain documents cited

Document D4:

D4: EP-A-0 982 304 (LILLY CO ELI) 1 March 2000 (2000-03-01)

can not be considered as prior art document under the Article 33(2) PCT, because it is published after the priority day and before the filing day of the application. However care should be taken by the applicant while entering the regional phase, because this document could be relevant for the examination, as it refers to similar piperidine derivatives having effects on serotonin related systems.